UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

MV

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,481	03/07/2006	Masahiko Kuroda	2006 0025A	7350

513 7590 04/19/2007

WENDEROTH, LIND & PONACK, L.L.P.
2033 K STREET N. W.
SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
GREENE, JAIME M	
ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,481	KURODA ET AL.	
	Examiner	Art Unit	
	Jaime M. Greene	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *2-5, 10-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6-8* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I in the reply filed on 2/20/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 2-5, 10-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/20/07.

Claim Objections

3. Claim 9 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only--, and/or, --cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

4. Claims 6, 7, and 8 objected to for depending from nonelected claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Applicant has chosen to use "means-plus-function" (or "step-plus-function") language in the claim(s), thereby invoking the special claim interpretation provisions of 35 USC 112, 6th paragraph, see MPEP 2181. According, wherever "means-plus-function" language is used in the claims, the claim is understood to encompass ONLY the specific means (or steps) described in the specification as corresponding to that part of the claim, and

equivalents of those specific means (or steps). See MPEP 2183 for discussion of equivalents in this context.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what the applicant considers as "high risk", as there is no explanation in the disclosure for what constitutes high risk for endometriosis-related disease, particularly as compared to risk in general. Applicant is required to clarify. Note that applicant may overcome this rejection by removing the word "high" from the claim.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 6, 7, and 8 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for endometriotic tissue, does not reasonably provide enablement for any biological sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

9. The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Teletronics Inc*, 8 USPQ2d

1217 (Fed Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986)) and *In re Wands* 8 USPQ2d 1400 (Fed. Cir. 1988)). These factors include the following:

(A) Level of predictability in the art. The art regarding correlating HRF expression levels with endometriosis in biological tissues must be considered unpredictable because the experiments were only performed in endometriotic tissues and the art provides no information about whether or not this correlation extends to other tissues.

(B) The state of the prior art. The state of the art with regard to HRF and endometriosis is poor, and of that prior art, expression levels of HRF are only correlated with endometriosis in endometriotic tissue and not in other unrelated tissues (See Oikawa, discussed herein below).

(C) Existence of working examples. Applicants present one example correlating HRF with endometriosis. Said example only examines RNA levels of HRF in endometriotic tissues as a means to correlate expression levels of HRF with endometriosis.

(D) Scope of the claims. The claims are broad and read on any biological sample, not just those containing endometriotic tissue.

(E) Amount of guidance provided. Applicants provide no guidance as to how to correlated HRF expression levels in tissues other than endometriotic tissues with endometriosis.

(F) Nature of the invention. The invention involves diagnosing endometriosis-related disease by preparing RNA from a biological sample, comparing the RNA expression

level of HRF from said sample with that of a normal sample, and using a determined increased HRF expression level as a means for determining if or the degree to which a subject has endometriosis-related disease.

(G) Level of skill in the art. The level of skill in the art is high; however, given the unpredictability in the art, the lack of guidance proved by applicants and the scope of the invention, it must be considered that the skilled artisan would have had to practice undue trial and error experimentation in order to practice the claimed invention according to the full scope of what is claimed.

Considering the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan would have been required to conduct undue experimentation in order to practice the claimed invention.

Note: Not all terms in a means-plus-function or step-plus-function clause are limited to what is disclosed in the written description and equivalents thereof, since 35 U.S.C. 112, sixth paragraph, applies only to the interpretation of the means or step that performs the recited function. See, e.g., *IMS Technology Inc. v. Haas Automation Inc.*, 206 F.3d 1422, 54 USPQ2d 1129 (Fed. Cir. 2000) (the term "data block" in the phrase "means to sequentially display data block inquiries" was not the means that caused the sequential display, and its meaning was not limited to the disclosed embodiment and equivalents thereof.).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claims 1, 6, and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by Oikawa (Oikawa, et al. Increased expression of IgE-dependent histamine-releasing factor in endometriotic implants. J Pathol. 2003 Mar;199(3):318-23). Claim 1 is drawn to a method of diagnosing endometriosis-related disease comprising: measuring the expression level of HRF polynucleotide in a biological sample from a subject, comparing HRF expression with a normal biological sample, and judging a subject with a significantly higher HRF level (as compared to normal) as having endometriosis-related disease or as being at high risk thereof. Claim 6 is drawn to a method for diagnosing endometriosis-related disease comprising: (a) preparing RNA from a biological sample of a subject; (b) subjecting the RNA from step (a) to an electrophoretic separation; (c) hybridizing the RNA of step (b) with the oligonucleotide probe of claim 3 under stringent conditions; (d) comparing the signal level of the oligonucleotide probe from step (c) with a normal sample; and (e) using a significantly higher HRF expression level when compared to normal as an index reflecting the degree of endometriosis-related disease or a risk thereof. Claim 8 is drawn to a method for diagnosing endometriosis-related disease comprising: (a)preparing RNA from a biological sample of a subject; (b) preparing cDNA from the primer set of claim 5 as a template; (c) comparing the level of

cDNA prepared in step (b) as a HRF polynucleotide index with a result of a normal sample; and (d) using a significantly higher HRF expression level when compared to normal as an index reflecting the degree of endometriosis-related disease or a risk thereof.

12. Regarding claim 1, Oikawa teaches a method of correlating endometriosis-related disease with HRF (diagnosing endometriosis-related disease) by measuring the expression level of HRF in a endometriotic implant tissues from three patients (biological sample from a subject; page 320), comparing HRF expression level with normal endometrial tissue (page 320), and suggesting that the overexpression of HRF in a sample may be sufficient for the acquisition of a growth advantage (i.e. judging a subject with a significantly higher HRF level (as compared to normal) as having endometriosis-related disease or as being at high risk thereof; page 322). Regarding claim 6, Oikawa teaches a method of correlating endometriosis-related disease with HRF by preparing RNA from endometriotic implants from patients (page 319); performing a Northern blot on said RNA using an HRF probe (i.e. subjecting the RNA to an electrophoretic separation and hybridizing the RNA with an labeled HRF oligonucleotide under stringent conditions); page 319); comparing the signal level of the oligonucleotides probe hybridized to RNA from the endometriotic tissue with the signal level from normal tissue (page 320, text and figure 1), and suggesting that the overexpression of HRF in a sample may be sufficient for the acquisition of a growth advantage (i.e. judging a subject with a significantly higher HRF level (as compared to normal) as having endometriosis-related disease or as being at high risk thereof; page

322). Regarding claim 8, Oikawa teaches a method of correlating endometriosis-related disease with HRF by preparing RNA from endometriotic implants from patients (page 319); performing RT-PCR on said RNA (i.e. preparing cDNA from the RNA; page 319); performing PCR on the cDNA and then performing a Southern blot using the PCR products from both the endometriotic implants and from normal tissue (i.e. comparing the level of cDNA prepared from the RNA as a HRF polynucleotide index with a result of a normal sample; page 319 and figure 1, page 320); and suggesting that the overexpression of HRF in a sample may be sufficient for the acquisition of a growth advantage (i.e. judging a subject with a significantly higher HRF level (as compared to normal) as having endometriosis-related disease or as being at high risk thereof; page 322).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1, 6, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oikawa as applied to claims 1, 6, and 8 above, and further in view of Fujise (Fujise, et al., US Patent Application Publication Number 2003/0172388). Claims 1, 6, and 8 are described above. Claim 7 is drawn to a method for diagnosing endometriosis-related disease comprising: (a)preparing RNA from a biological sample of a subject; (b)

preparing cDNA from the RNA of step (a); (c) contacting the labeled cDNA of step (b) with the microarray of claim 4; (d) comparing the signal level of the labeled cDNA as an index of HRF exp level with the result of a normal sample; and (e) using a significantly higher HRF expression level when compared to normal as an index reflecting the degree of endometriosis-related disease or a risk thereof. Oikawa teaches all the limitations of claims 1, 6, and 8, as described above, and thereby teaches preparing RNA from a biological sample of a subject; (b) preparing cDNA from the RNA of step (a) as described above.

While Oikawa does teach using nucleic-acid based techniques for the comparison of expression level of HRF in endometriotic and normal tissues (steps (d) and (e) of claim 7), Oikawa does not teach contacting the labeled cDNA of step (b) with the microarray of claim 4. However, Fujise teaches using fixed probe arrays (i.e. a microarray having an HRF polynucleotide as a target capture probe) as a means of looking at the differential expression of fortilin (i.e. HRF) between tissues (page 34, paragraphs 336 and 338 and page 35, paragraph 346). One of ordinary skill in the art would be motivated to use a microarray as a means of determining the expression levels of HRF for diagnostic purposes because microarrays provide quantitative results rapidly and accurately (page 35, paragraph 346), and there is a reasonable expectation of success because use of microarray technology is a standard technique in the art for analyzing RNA expression levels of virtually any RNA in any organism. Therefore it would have been prima facie obvious as the time the invention was made to utilize methods for detecting the expression level of HRF (including microarrays, RT-PCR,

Southern blotting, Northern blotting, etc.) in endometriotic tissue and comparing those levels with HRF expression levels in normal tissues as a means of diagnosing or assessing risk for endometriosis-related disease, absent evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jaime M. Greene whose telephone number is 571-270-3052. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JMG 4/3/07

DANIEL M. SULLIVAN, PH.D.
PRIMARY EXAMINER